1 of 4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE: YODER, et al.	)
	)**APPEAL NO. _____**
SERIAL NO: 09/772,603	)
	)
FOR: ISOLATED BOVINE IgG HEAVY CHAIN PROTEIN AND ITS USE AS AN ANTIMICROBIAL	))))**BRIEF ON APPEAL**
	)
	)
FILED: January 30, 2001	)
	)
	)
GROUP ART UNIT: 1644	)

To the Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sirs:

Please enter the following Brief on Appeal into the record.

I. INTRODUCTION

This is an appeal of the Final Rejection dated May 7, 2002, finally rejecting claims 8-10. The appealed claims 8-10 are set forth in an attached Appendix.

II. REAL PARTY OF INTEREST

The real party of interest in the present appeal is The Lauridsen Group, Inc.

III. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

IV. STATUS OF CLAIMS

Claims 1-10 were originally submitted January 30, 2001. In a response dated July 25, 2001, Appellants elected to prosecute claims 8-10 and cancel claims 1-7 as a result of a restriction requirement. In an amendment dated January 17, 2002, Appellant amended claim 8.

The claims here appealed are claims 8-10.

V. STATUS OF AMENDMENTS

Appellants did not file any further amendments following the final rejection. A Notice of Appeal was timely filed on August 7, 2002.

VI. SUMMARY OF INVENTION

The present invention relates to a unique, new protein isolate from the IgG fraction, which is an acid hydrolyzed IgG fraction that has been heat treated for from 15 minutes to 1 hour at a temperature of from 35°C to 40°C to unfold and modify the protein, making it antimicrobial in a manner not achievable by the original, untreated and unisolated IgG concentrate. (Specification page 3, lines 17-22). This protein has independent characteristics that are significantly different from the protein from which it was derived. (Spec. p. 4, lines 4-6). In addition to its significant physical characteristics, the bioactivity of the protein, when used against seven enteric bacterial strains, shows that the new protein is bacterial static when incorporated into bacterial media that are appropriate for the test organisms. (Spec. p. 4, lines 6-11). The growth of the test organisms, for example, has been reduced from 47.5% to 99.9% compared with controls. (Spec. p. 4, lines 11-13). In tissue cultures that had been impregnated with the test protein and infected with four selected virus strains, the test protein reduced virus growth from 95% to 100% compared with the controls. (Spec. p. 4, lines 13-16).

The invention provides for the first time a method where an essentially pure protein was separated from bovine IgG concentrate which, when the protein was evaluated using the SDS-page electrophoresis, was shown to produce an intact protein that had a significantly different molecular weight than the starting material, but yet appears to be an intact, nearly pure protein. (Spec. p. 4, lines 17-23). The desired fraction has a molecular weight of about 55,000, and can be used in liquid form, spray dried, or used with a suitable carrier, depending upon how and to whom it is dosed. (Spec. p. 5, lines 24-28).

The derived protein tested negative to a standard antigen-antibody reaction that is consistent with bovine IgG concentrate. The protein was destroyed when heat denatured. This protein, when tested with 3 strains of pathogenic E. Coli, 2 strains of Salmonella, one of Pasteurella and Streptococcus was bacterial static. When the same material was tested against 4 virus strains, it was viral static. (Spec. p. 4, lines 25-30). Also, the bovine IgG concentrate, when sterile filtered and tested to determine if the intact bovine IgG protein was bacteria static like the acid treated soluble fraction, showed the whole protein concentrate was not bacteria static. (Spec. pp. 4-5, lines 32-33 and 1-3, respectively).

In use with domesticated livestock animals, it has been found that an amount should be dosed sufficient to provide a dosage of about 0.25 mg/ml of volume in the mammal's gut. (Spec. p. 5, lines 29-31). Multiple dosing can occur with up to 5 grams/day. (Spec. p. 5, line 32).

VII. ISSUES

The issues on appeal are:

A. Whether claims 8-10 are unpatentable since the numbering of the claims is not in the left margin, and in view of the blank on p. 5, line 8.

B. Whether claim 8 is indefinite due to the recitation of "a mammalian species" in view of the fact that "mammal" has a commonly understood meaning.

C. Whether claim 8 is indefinite due to the recitation of "and" in line 1 in view of the fact that the ordinary meaning of the claim is that the IgG fraction of the present invention is effective against both bacteria and viruses.

D. Whether claims 8-10 are obvious over U.S. Pat. No. 6,096,310 (Bier) or U.S. Pat. No. 5,871,731 (Sprotte) each in view of Kempf et al. under 35 U.S.C. § 103(a) since the cited reference, even in combination, do not teach or suggest the use of a hydrolyzed, neutralized IgG fraction for providing bacterial static and viral static activity.

VIII. GROUPING OF THE CLAIMS

Claims 8-10 stand or fall together.

IX. ARGUMENT

A. Claims 8-10 are Not Rendered Unpatentable Due to the Positioning of the Claim Numbering or the Inclusion of a Blank in the Application

The Examiner has objected to the disclosure on the basis that: (1) the numbering of claims is in the center of the page rather than the left margin; and (2) due to the blank on page 5, line 8 that is not filled in.

With respect to (1), Appellants are unaware of a requirement in the MPEP or otherwise that patent claims must be numbered in the left margin of the page. The content of the claims is as easily understood with the claim number in the center of the page as in the left margin. Appellants therefore respectfully submit that the Examiner's objection in this regard is not well founded.

With respect to (2), the blank on page 5, line 8 of the application is to eventually fill in the patent number of Appellants' product sold under the trademark NUTRAGAMMAX™. Since the patent on this product has not yet issued, Appellants have not yet been able to fill in this number. It is respectfully submitted that the use of the blank does not impede understanding of the claimed invention by a person skilled in the art.

B. Claim 8 is Sufficiently Clear Such that Persons Skilled in the Art Can Determine Its Meaning with a Reasonable Degree of Precision and Particularity

1. The Law of Definiteness under 35 U.S.C. § 112, Second Paragraph

The standard for definiteness under 35 U.S.C. § 112, second paragraph is one of reasonableness under the circumstances. See e.g. Charvat v. Commissioner of Patents, 503 F.2d 138, 147-151 (D.C. Cir. 1974). The issue is whether, in the light of the teachings of the prior art and of the particular invention, the claims set out and circumscribe a particular area with a reasonable degree of precision and particularity. In re Moore, 439 F.2d 1232, 1235 (CCPA 1971). In determining indefiniteness, the claim language must be read in the light of the prior art and the teachings of the specification. See e.g. In re Moore, 439 F.2d 1232 (CCPA 1971). As stated by the CCPA (the predecessor to the Federal Circuit) in Moore:

> This...inquiry...is merely to determine whether the claims do, in fact, set out and circumscribe a particular area with a reasonable degree of precision and particularity...[T]he definiteness of the language must be analyzed - not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art.

Id. at 1235.

2. A Person Skilled in the Art Can Readily Ascertain the Scope and Meaning of "A Mammalian Species"

The Examiner has rejected claim 8 on the basis that the recitation of "a mammalian species" is indefinite and ambiguous. In this respect, the Examiner states that it is not clear which species Appellants intend to claim, since the phrase "includes not just livestock but also whale, for example."

It is respectfully submitted that the term "mammalian species" is not indefinite, since its definition is well known in the art and otherwise. While the Examiner infers that certain species of mammals were intended to be excluded from the commonly known definition of the term for use in the invention, such is not the case.

Since the term "mammalian species" sets out and circumscribes a particular type of animal with a reasonable degree of precision and particularity, the use of this phrase in claim 8 does not render it indefinite.

3. The Examiner's Interpretation of the Use of "And" in Claim 8 is Unreasonable

The Examiner next asserts that the use of "and" in claim 8, line 1 is ambiguous on the basis that "a mammal is more likely to have either bacterial or viral infection at any given time but not both at the same time." (Paper No. 8, p. 2). The phrase at issue is, "A method of providing bacterial static and viral static activity..." This rejection is nonsensical, since the claim language does not imply that the animal species must have both a bacterial infection and a viral infection at the same time. Instead, it simply states that the IgG fraction of the present invention is effective against both bacteria and viruses. This interpretation is supported on page 4, first paragraph of the specification wherein it describes that the new protein was found to be bacterial static when incorporated into bacterial media, and viral

static when impregnated into tissue cultures infected with selected virus strains. Thus, claim 8 is not indefinite, and the Examiner's rejection in this respect should be reversed.

C. Claims 8-10 are Not Rendered Obvious by Bier '310 or Sprotte '731 in View of Kempf et al. Under 35 U.S.C. § 103(a)

Claims 8-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bier '310 (U.S. Patent No. 6,096,310) or Sprotte '731 (U.S. Patent No. 5,871,731), both in view of Kempf et al. (Transfusion 31(5): 423-27; 1991). The Examiner asserts that one having ordinary skill in the art at the time the invention was made would have been motivated with a reasonable expectation of success to provide oral dosing of a mammalian species with isolated purified immunoglobulin because Bier '310 teaches oral dosing of immunoglobulin (IgG) such as bovine gamma globulin can provide bacterial static activity for gastrointestinal bacterial overgrowth. The Examiner further states that Sprotte '731 teaches oral administration of purified immunoglobulin to human at dosages from 1 to 20 g per day for several days to weeks for treatment of chronic pain associated with bacterial exposure, citing column 4, lines 36-47 in support. Finally, the Examiner alleges that Kempf et al. teach that mild acid hydrolysis at pH 4 with HCl, heat at a temperature of 37°C and neutralized with NaOH can inactivate viral activity, i.e. viral static activity, for the production of intravenous immunoglobulin, citing page 424, Fig. 1 in support. Appellants respectfully traverse this rejection.

1. The Law of Obviousness

The PTO bears the burden of establishing a case of prima facie obviousness. In re Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988). The critical inquiry for obviousness is whether "there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." Fromson v. Advance Offset Plate, Inc., 755 F.2d

1549, 1558 (Fed. Cir. 1985). In other words, obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." In re Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988), quoting ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577 (Fed. Cir. 1984). This suggestion cannot stem from the applicant's own disclosure, however. In re Ehrreich, 590 F.2d 902 (CCPA 1979).

2. The Combination of the Cited References Fail to Teach or Suggest Appellants' Claimed Method of Orally Administering an Acid-Hydrolyzed Fraction of IgG

Claim 8 from which claims 9-10 depend, describes a method of orally dosing a mammal with an IgG fraction that has been acid hydrolyzed for 15-60 minutes at 35-40°C, then neutralized. Claim 8 further provides that the IgG fraction is dosed in an antibacterial and antiviral amount. Appellants have surprisingly discovered that this IgG fraction has independent characteristics that are significantly different from the intact IgG protein. (Spec. p. 4, first para.). In addition to having a significantly different molecular weight, the new protein has been found to be bacterial static against numerous bacterial strains, as well as effective in reducing virus growth in infected tissue cultures. (Spec. p. 4, first para.). In contrast, the whole protein concentrate was not found to be bacteria static. (Spec. bottom of p. 4 to top of p. 5).

Bier '310 teaches oral administration of immunoglobulins for treating gastrointestinal bacterial overgrowth. The immunoglobulins used in Bier's method are whole and intact, and isolated using methods that are "well known in the art." (Col. 3, lines 35-39).

Similarly, Sprotte '731 teaches oral administration of whole and intact immunoglobulins for treatment of chronic pain syndrome. (Abstract). Sprotte '731 also

notes that the immunoglobulins of his invention are isolated and prepared using "known techniques." (Col. 2, lines 61-65).

Thus, Bier '310 and Sprotte '731 do not teach oral administration of an acid hydrolyzed, heated, and neutralized IgG fraction, as required by Appellant's claims. In fact, the Examiner admits that the cited references differ in this respect:

> The claimed invention as recited in claims 8 differs from the reference only by the recitation of said isolated IgG fraction which is acid hydrolyzed, and has been heat treated from 15 minutes to one hour at a temperature of 35°C to 40°C and thereafter neutralized.

(Paper No. 8, p. 4, para. 4).

While the Examiner flippantly notes that the claimed invention only differs from Bier and Sprotte in these respects, it is these treatment steps that are critical in producing Appellants' protein fraction having bacteria static and viral static properties. As already noted, Appellants' have demonstrated that IgG protein that has not been treated in this claimed manner does not have the requisite bacteria static properties. The Examiner dismisses Appellants' arguments in this regard, stating that, "the features upon which [Appellants] relies (i.e., IgG fraction is acid hydrolyzed to 55,000 MW protein prior to injection) are not recited in the rejected claim(s). (Paper No. 8, p. 3, point 8). However, this argument is baseless, since Appellants' claimed method that includes treatment of IgG protein with acid hydrolysis, heat, and neutralization, inherently produces an IgG fraction having a lower molecular weight than the whole, unmodified protein of Bier and Sprotte.

The Examiner cites Kempf et al. for the teachings missing from Bier and Sprotte, i.e. treatment of IgG with acid, heat, and neutralization using NaOH. Kempf, however, teaches the use of these method in the preparation of intravenous immunoglobulin. (See Title and

Abstract). Kempf notes that one of the primary problems associated with intravenous administration of blood and plasma derivatives include the transmission of viruses, such as HIV and hepatitis C. (Page 423). Kempf therefore describes methods of inactivating viruses in immunoglobulin solutions prior to intravenous administration in order to improve their safety. (Page 423). One of these methods disclosed by Kempf includes pretreatment of immunoglobulin solutions at pH 4 and a temperature of 37°C in the presence of pepsin in order to inactivate the viruses. (Page 423).

Contrary to the Examiner's assertion, there would have been no incentive for a person skilled in the art at the time of Appellants' invention to use the Kempf method of treating immunoglobulin for intravenous administration treatment in a method for oral dosing of immunoglobulin, as taught by Bier '310 and Sprotte '731. As already noted, the purpose of the Kempf treatment method is to reduce the risk of transmitting viruses through intravenous administration of immunoglobulin solution by inactivating viruses in the solution prior to administration. It is scientifically well established that transmission of the viruses as issue in Kempf et al., such as HIV, hepatitis B, hepatitis C, is through "intimate" routes, such as blood to blood (i.e. intravenously) or semen to blood contact. Kempf et al. note that "there have been several reports of the transmission of non-A, non-B hepatitis (hepatitis C) by immunoglobulin preparations intended for intravenous uses (IVIG)." However, such risks do not exist for the oral preparations of Bier '310 and Sprotte '731.

Therefore, there would not have been any incentive present for a person skilled in the art to combine the virus inactivation method disclosed by Kempf et al. in the oral immunoglobulin compositions of Bier '310 and Sprotte '731. Absent this suggestion, the Examiner has failed to provide a prima facie case of obviousness.

Appellants would further note that Bier '310 actually teaches away from its combination with Kempf et al. and its viral inactivation techniques. Bier '310 teaches oral administration of immunoglobulins derived from animal blood, plasma or serum. (Col. 1, lines 5-8). Bier '310 notes that the use of immunoglobulins derived from animals is advantageous since animals, such as cows, horses, pigs, sheep, and goats, do not carry "very serious disease vectors, including hepatitis and HIV." (Col. 2, lines 46-57). Thus, since the source of the Bier '310 immunoglobulins is already "safe", there would be no motivation whatsoever for a person skilled in the art to combine its teachings with the viral inactivation methods of Kempf et al.

3. Conclusion as to Obviousness

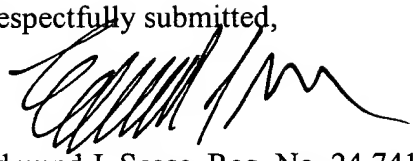
For all of the above-stated reasons, the claimed invention is not rendered obvious by The Examiner's rejection in this respect should therefore be reversed.

X. CONCLUSION

For the above-stated reasons, it is submitted that the claims are in a condition for allowability. The decision of the Examiner, therefore, should be reversed and the case allowed.

Enclosed herein please find the appeal brief in triplicate, required fee of $155, and request for oral argument. If the fee amount is not correct, please consider this a request to debit or credit Deposit Account No. 26-0084 accordingly.

Respectfully submitted,



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APPENDIX

8.

A method of providing bacterial static and viral static activity, comprising:

oral dosing of a mammalian species with an anti-bacterial and antiviral effective amount of a treated, isolated and neutralized IgG fraction which has been treated by acid hydrolysis, heated from 15 minutes to 1.0 hour at a temperature of 35°C to 40°C and thereafter neutralized.

9.

The method of claim 8 wherein the amount dosed is sufficient to provide a dosage of 0.25 mg/ml in the mammal's gut.

10.

The method of claim 8 wherein the dose is up to 5 grams/day.